REMARKS

Claims 1-5, 15, 16, 47, 48, 86-89 and 98 are pending. Claim 5 has been cancelled. Claims 15 and 98 have been amended to include a sampling time statement and to clarify that the subsequent sample is from the original subject. Support for the amendments is found at least at page 28, lines 18-25 of the specification as filed. Claims 4 and 88 have been amended to clarify the meaning of the fragments. Support for the amendment is found at least in claims 4 and 88 as filed. No new matter has been added.

Summary of Telephone Conference with Examiner

Applicant acknowledges that Applicant's representative conducted a telephone interview with Examiner C.D. Ly on April 3, 2003 during which an election of SEQ ID NOs:1 and 5, which encode polypeptides SEQ ID NOs:16 and 20, was made. Applicant agrees to the election, but maintain the traversal of the sequence election requirement because, while acknowledging that the nucleotide sequences encoding different proteins are different, the claims are directed to methods for using the sequences in the diagnosis of cancer. Therefore, Applicant does not believe that examination of the recited sequences as used in the methods would entail a significant burden on the Examiner.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 4, 5, 15, 47, 48, 88 and 98 under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner rejected claims 4 and 88 based on the use of the phrase "antigen-binding fragment thereof." Applicant has amended the claim to clarify that the phrase "antigen-binding fragment thereof" means antigen-binding fragment of an antibody. On the basis of the amendment, Applicant believes the rejection has been obviated.

Accordingly, withdrawal of the rejection of claims 4 and 88 under 35 U.S.C. §112, second paragraph, is respectfully requested.

The Examiner rejected claim 5 as indefinite based on the inclusion of the phrase "colon cancer-associated polypeptides other than those encoded by". Applicant has cancelled the claim.

The Examiner rejected claims 15, 16, and 98 as being indefinite with respect to the times at which the samples are obtained. Claims 15 and 98 have been amended as suggested by the Examiner to include a sampling time statement. Applicant submits that the amendment to the claim obviates the rejection and request that the rejection of claims 15, 16, and 98 under 35 U.S.C. §112 be withdrawn.

The Examiner rejected claim 47 as indefinite based on the inclusion of the phrase "one or more control antigens" in the claim. Applicant respectfully traverses the rejection.

The Examiner is apparently unsure of the meaning of the phrase "control antigen". Applicant respectfully submits that the term "control" is a term of art and that the phrase "control antigen" would be understood by one of ordinary skill to be an antigen that is included in the claimed kit to as a test antigen to ensure the kit components are functional and perform properly. For example, a control antigen included in a kit would be used as a control sample when one utilized the kit to test for antigens in a biological sample. The control antigen would be put into an identically prepared blank sample and that control sample would be reacted with the colon cancer-associated polypeptides of the kit in parallel to, and under the same conditions used with the test biological sample. The control antigen provides a way to monitor experimental factors such as reagent quality, background signal, etc. An example of use of a control peptide in methods of the invention can be found at page 31, lines 3-6, which describes the use of a control peptide to determine factors such as peptide or protein quality and binding characteristics, reagent quality and effectiveness, hybridization (in this case binding) success, and analysis thresholds and success.

Applicant respectfully submits that claim 47 is not indefinite because the term "control" is a term of art that would be understood by one of ordinary skill, and because the specification also provides details relating to the use of controls in the methods of the claimed invention. Therefore, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claim 47 under 35 U.S.C. §112, second paragraph.

The Examiner rejected claims 15, 16, and 98 as indefinite based on the use of the word "a" with respect to the subject from which the second biological sample obtained. Applicant has amended claims 15 and 98 to replace the word "a" with the word "the" to clarify that the subsequent sample is obtained from the same subject as the initial sample. Applicant submits that the amendment obviates the rejection and requests the Examiner withdraw the rejection of claims 15 and 98 under 35 U.S.C. §112 second paragraph.

Rejections under 35 U.S.C. §101

The Examiner has rejected claims 1-5, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. §101 because the claimed invention allegedly is not supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility. Applicant respectfully traverses the rejection.

According to 35 U.S.C. §101, an invention to be patentable must have one or more utilities, which has been interpreted to mean that either a specific and credible utility, or a well-established utility must be provided in a patent application. *Manson v Brenner* 383 U.S. 519, 148 USPQ 689 (1966); *Nelson v Bowler* 626 F.2d 853, 206 USPQ 881 (C.C.P.A. 1980). Establishment of one utility is sufficient to meet the statutory utility requirement. *Rey-Bellet v Englehardt* 493 F.2d 1380, 1383, 181 USPQ 453, 454 (C.C.P.A. 1974). As defined in the Revised Interim Utility Guidelines Training Materials quoted by the Examiner, a substantial utility is "a practical utility which defines a 'real world' context of use." The PTO Training Materials state that credible with respect to utility means that "the utility is believable to a person of ordinary skill in the art" and that further that the term "refers to the reliability of the assertion of utility based on the logic and facts offered by applicant to support the assertion." As defined in the PTO Training Materials, a well-established utility is "a specific, substantial, and credible utility which is well known, immediately apparent or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art." A specific utility is one that is "specific to the subject matter claimed," as opposed to general utility applicable to the broad class of the invention.

Applicant has provided one or more utilities that are substantial, credible and specific to the claimed invention. Based on the knowledge of one of ordinary skill in the art, the disclosed utilities are also well established. The description of the nucleic acid molecules in the

specification, coupled with the methodology used to isolate the nucleic acid molecules, makes immediately apparent to one of ordinary skill in the art at least one specific, substantial and credible utility overlooked by the Examiner. For example, the nucleic acid molecules and polypeptides encoded by the nucleic acid molecules can be used in claimed methods for the diagnosis of colon cancer and/or assessment of treatment of colon cancer in a subject.

More specifically, the disclosed nucleic acid molecules can be used in the claimed methods to generate encoded polypeptides that are useful in for the diagnosis of colon cancer and for assessment of colon cancer therapeutic methods, particularly in the identification of individuals having specific antibodies that bind to the encoded polypeptides. That the nucleic acid molecules disclosed in the application encode polypeptides recognized by antibodies in the sera of individuals with colon cancer is known by virtue of the method by which the nucleic acid molecules were isolated (SEREX).

Accordingly, in view of the knowledge of one of ordinary skill in the art with respect to SEREX and antibody recognition, Applicant asserts that at least one utility provided in the application is credible, specific, and substantial. Applicant bases this assertion on the utility definitions provided by the Examiner in the Office Action.

Credible utility. The use of nucleic acid molecules to produce proteins is well known and currently available technology. The use of such produced proteins to bind specific antibodies in a variety of immunoassays is well known and currently available. Accordingly, the asserted utility is credible.

Specific utility. The disclosed utility relates to the diagnosis of colon cancer using the disclosed proteins that are specifically recognized by antibodies produced by individuals with colon cancer. The existence of an immune response against specific proteins of cancer cells is well known. The specificity of the immune response, i.e., antigen-antibody binding, is also well known. The diagnosis of cancer based on antigen-antibody binding is well known. The specific diagnostic utility described in the application is specific for the disclosed nucleic acid molecules and the polypeptides encoded by the nucleic acid molecules. The recognition of the encoded polypeptides by antibodies in patient antisera is disclosed in the application. The specificity of the diagnostic methods for colon cancer is disclosed in the application. The utility does <u>not</u> relate to an "unspecified" disease.

Substantial utility. The disclosed utility is substantial because it is "an assay that measures the presence of a material [antibodies] which has a stated correlation to a predisposition to the onset of a particular disease condition [colon cancer]. Note that the disclosed utility, diagnosis of colon cancer by determining antigen-antibody recognition, is a "real world" use practiced daily in clinics around the world. Applicant's disclosure provides additional proteins that are specifically recognized by the human immune system and thus useful in "real world" diagnostic applications.

Applicant further notes that the disclosed utility fits within the definition of "well-established" utility provided by the Examiner. As described above, the utility of using the nucleic acid molecules to produce polypeptides for use in specific assays of immune responses in cancer is specific, substantial, credible, and well known by those of ordinary skill in the art. The utility also would be immediately apparent of one of ordinary skill in the art based on the teachings of the specification and in view of the knowledge of one of ordinary skill in the art.

Applicant disagrees with the Examiner's statement that "the protein produced as a final product resulting from processes involving the nucleic acid does not have asserted or identified specific and substantial utilities." (Office Action at page 6) The Examiner's assertions that none of the asserted utilities are specific or substantial because such utilities are "generic in nature and applicable to many such components" (Office Action at page 6) cannot be considered as accurate in view of the utilities discussed above. The use of the proteins encoded by the nucleic acids in the diagnosis of a specific disease, colon cancer, is hardly a use that is applicable to "many" proteins.

Moreover, the Examiner's assertions that "The SEREX method requires antigen to be identified via sequence comparisons with either the EMBL or GenBank databases. Absent factual evidence, one skilled in the art would have reasons to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence" (Office Action at page 7) are not relevant to the question of utility. Applicant respectfully asserts that the invention relates to the use of colon cancer-associated antibodies that have been determined to recognize colon cancer-associated polypeptides. Aside from the demonstrated ability of the antibodies to specifically bind to colon cancer-associated polypeptides in a sample as an indication of colon cancer, it is not necessary to delineate any other function of the polypeptides. Thus, the Examiner's

arguments relating to unpredictability of the relationship between sequence, structure, and function of the polypeptides is not relevant to the utility of the claims of the invention.

The utility of the claims is based in part on the determination that the polypeptides set forth as SEQ ID NOs:16-30, which are encoded by nucleic acids set forth as SEQ ID NOs:1-15, are not recognized by sera from normal patients. In summary, the data supplied in the specification makes it clear that the polypeptides encoded by these nucleic acid molecules are not recognized by the immune systems of the normal individuals tested, but are recognized by the immune systems of persons having colon cancer (see Example 1). Accordingly, one of ordinary skill in the art would readily recognize these nucleic acids and proteins as having utility in the diagnosis of colon cancer. Thus, the working examples directly contradict the Examiner's reasons for asserting a lack of specific, credible or substantial utility. Therefore, the Examiner has not met the burden for a *prima facie* showing of lack of utility for the claimed invention, and it is respectfully requested that the rejection claims 1-5, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. § 101 for lack of utility be withdrawn.

Rejections Under 35 U.S.C. §112, first paragraph

Enablement

The Examiner rejected claims 1-5, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. §112, first paragraph for lack of enablement. Applicant respectfully traverses the rejection and asserts that the claimed invention is enabled throughout its scope.

As stated in the MPEP §2164.04, the burden is on the Examiner to establish a *prima facie* case when making an enablement rejection. In the Office Action at pages 8 and 9, the Examiner indicates that the enablement rejection of claims 1-5, 15, 16, 47, 48, 86-89, and 98 is based on factors set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (CAFC 1988), which are to be considered in determining whether undue experimentation is required for enablement. To establish a *prima facie* case for lack of enablement, the case law indicates that, "the examiner's analysis must consider all of the evidence related to each of these factors, and any conclusion of non enablement must be based on the evidence as a whole. *In re Wands*, 858 F.2d 731, 737, 740, 8 USPQ2d 1400, at 1404, 1407 (CAFC 1988). Thus, the burden is on the Examiner to present evidence that is sufficient to support the Examiner's conclusion regarding a lack of enablement

of the claimed invention, and to put forth the requisite *prima facie* case for lack of enablement, "specific, technical reasons are always required" (MPEP §2164.04).

Applicant respectfully submits that the Examiner not presented any evidence, specific or otherwise, indicating a of lack of enablement of the claimed invention and therefore has failed to meet the burden necessary to support an enablement rejection. Instead, the Examiner has merely referred to the utility rejection made in this Office Action. In addition to being insufficient on its face to make a *prima facie* case of non-enablement, this rejection is based on an unfounded utility rejection, as demonstrated above. Applicant therefore respectfully requests the Examiner to withdraw the rejection of claims 1-5, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. §112 first paragraph.

Written Description

The Examiner rejected claim 5 under U.S.C. §112, first paragraph as lacking adequate written description. Applicant has cancelled claim 5.

Information Disclosure Statement

Applicant resubmits herewith a replacement copy of each of the documents previously filed with the Information Disclosure Statement and PTO-1449 form filed February 10, 2003. Applicant respectfully requests entry of the documents into the file and consideration by the Examiner.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee

occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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